

Appl. No. : **10/712,795**
Filed : **November 13, 2003**

SUMMARY OF INTERVIEW

Identification of Claims Discussed

Claims 109-145 were discussed.

Principal Arguments and Other Matters

Applicants' representatives discussed with the Examiner potential amendments that would put the claims in condition for allowance.

Results of Interview

It was agreed that amending claim 1 to replace nucleotide range 3230-3288 with the range 3249-3268 would overcome the rejection under 35 U.S.C. § 112, first paragraph and would likely overcome the rejections based on prior art.

Appl. No. : **10/712,795**
Filed : **November 13, 2003**

REMARKS

Applicants wish to thank Examiner Epps-Ford for the time and courtesy extended during the personal interview conducted on April 28, 2006.

Status of Claims

Claims 109-212 are currently pending. Claims 1-108 have been canceled and claims 146-196 are withdrawn without prejudice or disclaimer. Applicants reserve their right to pursue the subject matter of any or all of these claims in one or more continuing applications.

Amendments to the Specification

Amendments to the specification were made to assign sequence identifiers to sequence disclosures, and to correct errors in the sequence disclosures identified below. No new matter is introduced by way of these amendments.

Sequence Disclosures

The nucleotide sequences found on page 179, at lines 20-31, have been assigned appropriate sequence identifiers, and the Sequence Listing has been amended accordingly. Additionally, the specification has been amended at page 206 such that the sequence disclosures in Tables 33 and 34 are assigned appropriate sequence identifiers and comply with the requirements of 37 CFR 1.821 through 1.825. The Sequence Listing has been amended accordingly.

Amendments to Table 33

Further amendments are submitted herewith to correct errors in the sequences listed under the Table 33 heading "ISIS 301012 target sequence." In the first row, labeled "human", the ISIS 301012 target sequence has been amended to delete an "a" from the 5' end of the sequence and insert a "c" at the 3' end of the sequence, such that the sequence now reads "ggtgcgaagcagactgaggc." The human ISIS 301012 target sequence as amended has the nucleobase sequence of SEQ ID NO: 614, which corresponds to nucleotides 3249-3268 of SEQ ID NO: 3 and was provided in Table 18 in the specification as filed.

Similar amendments were made to the ISIS 301012 target sequences listed in the row labeled "monkey" and the row labeled "mouse". The monkey ISIS 301012 target sequence was amended to delete an "a" from the 5' end of the sequence and insert a "c" at the 3' end of the sequence, such that it now reads "ggtgtaaagcagactgaggc." As is readily apparent from a

Appl. No. : **10/712,795**
Filed : **November 13, 2003**

comparison of the ISIS 301012 target region of the human apolipoprotein B mRNA (SEQ ID NO: 3 of the instant specification) to the corresponding sequence in the monkey apolipoprotein B sequence provided in the instant specification (SEQ ID NO: 855), the monkey ISIS 301012 target sequence is the sequence as amended, "ggtgtaaagcagactgaggc." The monkey ISIS 301012 target sequence is now correctly listed as nucleotides 168-187 of SEQ ID NO: 855. Likewise, the ISIS 301012 target sequence in the row labeled "mouse" was amended to delete an "a" from the 5' end of the sequence and insert a "c" at the 3' end of the sequence, such that it now reads "ggagtgcagcagtctgaagc." As is readily apparent from comparison of the sequence of the human ISIS 301012 target sequence (SEQ ID NO: 3) to the corresponding sequence in mouse apolipoprotein B sequences (publicly available at the time of filing), the mouse ISIS 301012 target sequence is the sequence as amended, "ggagtgcagcagtctgaagc."

Amendments to Table 34

Amendments were made to the nucleotide sequences listed under the heading "ISIS 147764 binding site" in Table 34. In the specification as filed, the sequences of the ISIS 147764 binding sites were reversed; i.e. the row listing the human binding site was labeled "mouse" and the row listing the mouse binding site was labeled "human". As is readily apparent from comparison of the nucleotide sequences of ISIS 147764 to the mouse apolipoprotein B sequence provided in the instant specification (SEQ ID NO: 10), and from the target site of ISIS 147764 provided in Table 3, the sequence of the mouse ISIS 147764 binding site is "gcattgacatcttcagggac," which is provided in the amended Table 34 and corresponds to nucleotides 541-560 of SEQ ID NO: 10. Likewise, the sequence of the ISIS 147764 binding site in the human apolipoprotein B mRNA provided in the instant specification (SEQ ID NO: 3) is "gcatggacttctctgaaa," which is provided in the amended Table 34 and corresponds to nucleotides 8886-8905 of SEQ ID NO: 3.

Nucleotide mismatches in Tables 33 and 34 were identified by underscored text in the specification as filed. Nucleotide mismatches that are to remain underscored are indicated by double-underscored text. Insertions are indicated by single-underscored text.

Amendments to the Claims

Appl. No. : **10/712,795**
Filed : **November 13, 2003**

Claims 109 and 125 have been amended. Support for the claim amendments can be found throughout the specification. For example, support for amendments to claim 109 are found on page 8, at lines 1-4; on page 27, at lines 12-15; and on page 168, in Table 18; support for amendments to claim 125 is found on page 218, in Table 41. No new matter has been added by way of these amendments.

Claims 197-212 have been newly added and find support in the claims as originally filed and throughout the specification. For example, support for claims 197-212 can be found at page 169, in Table 18, and at page 148, in Table 11, and elsewhere throughout the specification. No new matter has been added by way of new claims.

Reconsideration of the pending claims in view of the amendments and comments presented herein is respectfully requested.

Inventorship

The Examiner has stated that in view of the papers filed March 3, 2006, the inventorship of the instant application has been changed by the addition of Susan Freier as an inventor.

Information Disclosure Statements

The Examiner indicated that the information disclosure statement filed on April 4, 2005 failed to comply with 37 C.F.R. § 1.98(a)(2), and as such documents other than US patent documents were not considered by the Examiner. Applicants filed a supplemental information disclosure statement on June 27, 2006 in order to provide copies of non-patent literature documents and foreign references. Applicants respectfully request consideration of these references by the Examiner.

Sequence Disclosures

In paragraph 8 of the Office Action mailed April 14, 2006, the Examiner pointed to sequence disclosures on page 206 of the specification that allegedly failed to comply with the requirements of the sequence rules as set forth in 37 C.F.R. § 1.821 through 1.825. The Examiner additionally referenced an attached "Notice to Comply with Requirements for Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures".

Appl. No. : **10/712,795**
Filed : **November 13, 2003**

However, the Office Action did not include such a notice, nor is one available through PAIR. Nevertheless, Applicants believe that the instant response represents a complete reply to the outstanding Office Action, and that the sequence disclosures contained within the specification are in compliance with the sequence rules in view of the foregoing amendments.

Response to Rejection under 35 U.S.C. § 112, first paragraph

The Examiner rejected claims 109-124 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Applicants respectfully disagree and assert that the claims meet the written description requirements under 35 U.S.C. § 112, first paragraph as presented. However, in an effort to advance prosecution, Applicants have amended claim 109 to replace nucleotide range 3230-3288 of SEQ ID NO:3 with nucleotide range 3249-3268 of SEQ ID NO:3. During the personal interview conducted on April 28, 2006, it was agreed that such an amendment would overcome the written description rejection. Accordingly, Applicants respectfully request withdrawal of the rejection.

Response to Rejection under 35 U.S.C. § 102(b) in view of Olek et al.

The Examiner rejected claims 109-112 under 35 U.S.C. § 102(b) as being anticipated by Olek et al. The cited reference allegedly discloses 2 oligonucleotides of 13 nucleobases in length, each of which comprises an 11 base pair contiguous stretch of nucleotides that is 100% complementary to nucleobases 3278 through 3288 of SEQ ID NO: 3. Applicants respectfully disagree that Olek et al. teach all of the elements of claims 109-112. Claim 109 as currently amended recites antisense compounds 12 to 30 nucleobases in length that (a) hybridize to nucleobases 3249 to 3268 of SEQ ID NO: 3 and (b) have no more than 2 mismatches with respect to SEQ ID NO: 3. The oligonucleotides disclosed by Olek et al. do not meet the limitations of claim 109 as amended and as such, claim 109 and the claims depending therefrom are not anticipated by Olek et al. Accordingly, the instant amendments obviate the rejection of claims 109-112 under 35 U.S.C. § 102(b) and Applicants respectfully request that the rejection be withdrawn.

Response to Rejection under 35 U.S.C. § 102(b) in view of Bennett et al.

Appl. No. : **10/712,795**
Filed : **November 13, 2003**

The Examiner rejected claims 109-115, 117-118, 120-126, 129-132, 134-135, and 137-141 under 35 U.S.C. § 102(b) as being anticipated by Bennett et al. The Bennett et al. reference discloses an antisense oligonucleotide 20 nucleobases in length that shares 13 identical nucleobases with SEQ ID NO: 247 of the instant application and comprises a region of 9 contiguous nucleobases that are 100% complementary to nucleobases 3258-3268 of SEQ ID NO: 3 of the instant application.

Applicants respectfully disagree with the Examiner's assertion that claim 109 is anticipated by SEQ ID NO: 22 of Bennett et al in that the cited oligonucleotide would not specifically hybridize with SEQ ID NO: 3 in the manner in which "specifically hybridize" is described in the specification. However, solely in an effort to advance prosecution, Applicants have amended claim 109 for clarity to recite that the antisense compounds (a) hybridize to nucleobases 3249 to 3268 of SEQ ID NO: 3 and (b) have no more than 2 mismatches with respect to SEQ ID NO: 3. SEQ ID NO: 22 contains five mismatches with respect to the nucleotide range recited in amended claim 109. Thus, claim 109, and the claims depending therefrom, are not anticipated by SEQ ID NO: 22 of Bennett et al.

Applicants have amended claim 125 to recite that the compounds are 14 to 30 nucleobases in length and comprise at least 14 contiguous nucleotides of SEQ ID NO: 247. Accordingly, claim 125, as well as the claims depending therefrom, are not anticipated by SEQ ID NO: 22 of Bennett et al.

Applicants submit that the instant amendments obviate the rejection of claims 109-115, 117-118, 120-126, 129-132, 134-135, and 137-141 under 35 U.S.C. § 102(b), and respectfully request withdrawal of the rejection.

Response to Rejection under 35 U.S.C. § 103(a)

The Examiner rejected claims 109-126 and 129-141 under 35 U.S.C. § 103(a) as being unpatentable over Bennett et al. in view of Peterson et al. Applicants respectfully disagree because, as discussed in the foregoing remarks, SEQ ID NO: 22 of Bennett et al. does not fall within the scope of claims 109 or 126 as currently amended. Thus, Applicants submit that this rejection is rendered improper because the cited references do not, either alone or in combination, teach or suggest all of the limitations in claims 109 and 126 or the claims

Appl. No. : **10/712,795**
Filed : **November 13, 2003**

depending therefrom. As such, the combination of the cited references does not render the pending claims obvious and Applicants respectfully request withdrawal of the rejection.

Response to Obviousness Type Double Patenting Rejection

The Examiner has provisionally rejected claims 109-141 on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 1-34 of copending Application No. 10/920,612. Applicants request that this rejection be held in abeyance until allowable subject matter is indicated.

Allowable Claims

Applicants note the Examiner's conclusion that Claims 142-145 are allowed.

Request for Rejoinder

In the Office Action mailed November 7, 2005, the Examiner required restriction between the product and process claims presented for examination at the time of filing. Following Applicants' election of product claims 109-145, the process claims 146-196, all of which depend from and incorporate the limitations of the product claims under examination, were withdrawn from further consideration by the Examiner. In accordance with the procedures set forth in MPEP § 821.04(b), Applicants request that previously nonelected process claims 180-196, depending from allowed claims 142-145, be rejoined and fully examined for patentability. Additionally, Applicants request that upon allowance of the remaining product claims 109-141, the previously nonelected process claims 146-179 be rejoined and fully examined for patentability.

CONCLUSION

Applicants believe that all outstanding issues in this case have been resolved and that the present claims are in condition for allowance. Nevertheless, if any undeveloped issues remain or if any issues require clarification, the Examiner is invited to contact the undersigned at the telephone number provided below in order to expedite the resolution of such issues.

Appl. No. : 10/712,795
Filed : November 13, 2003

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 50-0252.

Respectfully submitted,

Dated: July 14, 2006

By: Frances Putkey
Frances Putkey, Ph.D.
Registration No. 57,257
Customer No. 55,389

Isis Pharmaceuticals, Inc
1896 Rutherford Rd.
Carlsbad, CA 92008
(760) 603-2710 – Phone
(760) 603-3820 – Facsimile